REMARKS

Entry of the foregoing and further and favorable reconsideration consideration of the subject application on the merits is respectfully requested.

Applicants gratefully acknowledge the Examiner's indication that claims 39-41 and 50-52 are free of the prior art and would be allowable if rewritten in independent form. By the present Amendment, Applicants have rewritten claims 39 and 50 in independent form. Claims 1-31, 33, 35 to 37, 44, 46 to 48, 53 and 54 have been canceled without prejudice to or disclaimer of the subject matter claimed therein. Applicants reserve their right to file a continuation application directed towards the canceled subject matter. Claims 32, 34, 38, 39, 42, 43, 45, 49 and 50 have been amended. Support for the amendment of claims 32, 34 and 38 can be found at least at page 11, lines 3-6 and 25-30 and page 22 lines 27-29 of the specification as originally filed. Support for the amendment to claim 42 can be found at least at page 26, lines 5-10 of the specification as originally filed. Support for the amendment of claims 43, 45 and 49 can be found at least at page 19, lines 4-9 and page 22, lines 27-29 of the specification as originally filed. No new matter has been added by these amendments.

Election/Restriction

The Examiner has withdrawn claims 1-31 from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1-31, directed towards non-elected inventions, have been deleted by Applicants solely to expedite prosecution and without acquiescing to the Examiner's objection.

Priority

At pages 2-3 of the Official Action, the Examiner asserts that Applicants' priority claim in this case is defective, because

> Applicant's Declaration states that this application claims priority to application 09/294,022 under 35 USC§ 120, however this application was abandoned and re-filed as provisional application 60/219,314. Applicant's can not claim benefit to a provisional application under 35 USC § 120, this claim must be made under 35 USC § 119(e).

Applicants respectfully submit that the Examiner's statement of the facts surrounding their priority claim is not precisely correct. In fact, when their Declaration was executed, in May, 2000, priority application 09/294,022 was still pending. Consequently, the priority claim in the Declaration under 35 USC §120 was correct at the time the Declaration was signed. At that time, Applicants had filed a Petition to convert that application into a provisional application; that petition was granted later, on July 10, 2000. However, at the time the Declaration was signed, a priority claim under 35 USC §119(e) would have been inappropriate. Applicants also note that at no time was the priority application abandoned by Applicants in favor of any other application; only after Applicants' petition was granted did that application automatically go abandoned by operation of statute.

Without conceding that the priority claim in the present case is in any way defective, Applicants hereby express their willingness to provide a supplemental Declaration indicating the Serial Number of the now-provisional priority application in this case, upon indication by the Examiner that such a procedure will obviate the present objection.

Claim Rejections - 35 USC § 102

Claims 32, 34, 38, 42, 43, 45, 49, and 53-54 are rejected under 35 U.S.C. §102(b) as purportedly anticipated by Fitzmaurice et al. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

The Examiner argues, at pages 3-4 of the Official Action, that Fitzmaurice et al. describes "recombinant STMV RNA molecules containing exogenous RNA segments, . . . and a recombinant expression system making possible production of a desired gene product in the cytoplasm of a plant infected with recombinant STMV RNA molecules and a helper virus." The Examiner further argues that "[t]he exogenous RNA segments of [Fitzmaurice et al.] include those encoding different heterologous proteins, RNA having catalytic activity (*i.e.* ribozymes), regulatory function and may also be anti-sense RNA (page 13, lines 14-37)."

Without conceding to the Examiner's arguments, but solely in an effort to expedite prosecution, Applicants have amended independent claims 32 and 43 to recite that the inhibitory RNA comprises sense RNA. The Examiner has not included dependent claim 33, drawn to the introduction in a plant cell of inhibitory RNA comprising sense RNA, in this rejection over Fitzmaurice et al. It is respectfully submitted by the Applicants that Fitzmaurice et al. does not teach a method for introducing into the cytoplasm of plant cells recombinant RNA molecules derived from STMV ssRNA having sense RNA, thereby silence endogenous genes. Consequently, Applicants submit that Fitzmaurice et al. fails to teach all features of the amended claims 32 and 43 (and the claims that depend therefrom), and thereby does not anticipate the rejected claims. Applicants note that claims 53 and 54

have been deleted, rendering this rejection moot as it applied to these claims. In view of the above, withdrawal of this rejection is respectfully requested.

Claims 32, 34, 42, 43, 45, and 49 are rejected under 35 U.S.C. 102(b) as purportedly anticipated by Masuta et al. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

At pages 4-5 of the Official Action, the Examiner argues that "Masuta et al. relates to a novel vector constructed by inserting an exogenous RNA fragment into a vector comprising a satellite RNA of a plant virus . . . wherein said RNA vector comprises an exogenous gene integrated into the satellite RNA." The Examiner further argues that "[t]he satellite RNAs used in the invention of Masuta et al. are not limited to those derived from CMV, those having the same effect in spite of the difference in partial base sequence fall within the invention (col. 2, lines 30-33)."

Applicants respectfully point out that the CMV satellite RNAs of Masuta et al. are "satellite RNAs" and not "satellite viruses". "Satellite RNAs" and "satellite viruses" are clearly distinguished in the art, as pointed out by Masuta in col. 1 line 18-28. "Satellite viruses" are larger and comprise a gene encoding their own coat protein, while satellite RNAs are low molecular weight RNAs which are encapsidated within the viral particle of the helper virus (Masuta col.1 line 23-28 and col.4 line 22-25). Thus, even though the "satellite RNAs" of Masuta et al. may not be limited to those satellite RNAs of CMV, but may extend to variants of CMV satellite RNAs, namely those "having the same effect in spite of differences in partial base sequence" to CMV satellite RNAs, they do not extend to

"satellite viruses", such as STMV or STNV, which are completely distinct from "satellite RNAs".

Claims 32 and 43 refer to vectors derived from "satellite viruses". Applicants respectfully submit that Masuta et al. does not teach or suggest the use vectors derived from "satellite viruses", such as STMV or STNV derived viral vectors, for introduction of inhibitory RNA into a plant cell.

At page 5 of the Official Action, the Examiner argues further that the vectors of Masuta et al. "can be used to produce a virus-resistant plant by introducing the antisense sequence of a plant virus in the plant to transform it (col. 4, lines 38-40)." Without conceding to the Examiner's arguments, but solely in an effort to expedite prosecution, Applicants have amended claim 32 and 43 to refer to the silencing of an endogenous gene by the introduction of sense RNA into a plant cell. Applicants note that claim 33, drawn to the introduction in a plant cell of inhibitory RNA comprising sense RNA, is not included in the present rejection, and so is unequivocally not anticipated by Masuta et al. Further, it is respectfully submitted that Masuta et al. does not teach the introduction of inhibitory RNA into a plant cell, targeted to the silencing of endogenous plant genes. Applicants submit that Masuta et al. fails to teach all features of the amended claims 32 and 43, nor the claims that depend therefrom, and thus does not anticipate those claims. Accordingly, withdrawal of the rejection is respectfully requested.

Claim Rejections - 35 USC §103

Claims 32-38, 42-49, and 53-54 are rejected as purportedly obvious over Fitzmaurice et al., and Masuta et al. in view of Grierson et al. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

The deficiencies of Fitzmaurice et al. and Masuta et al. are set forth in detail above. The Examiner concedes, at page 5 of the Official Action, that neither Fitzmaurice et al. nor Masuta et al. "specifically teaches wherein the inhibitory RNA comprises an inverted repeat, nor do they teach wherein said inhibitory RNA comprises a complementary stretch of at least 50 or at least 100 nucleotides of sense and antisense RNA." However, at page 6 of the Official Action, the Examiner states that "Grierson et al. 'have found that the inhibitory effect of a gene silencing vector can be enhanced by creating in the vector an inverted repeat of a part of the sequence of the vector'." On this basis, the Examiner argues that "[o]ne of ordinary skill in the art would have been motivated to modify the gene silencing constructs of Fitzmaurice et al., And Masuta et al. by incorporating one or more inverted repeats into these constructs since the teachings of Grierson et al. are cleary expected to have enhanced properties in comparison to unmodified constructs."

First, Applicants note that while not conceding to the Examiner's arguments, but solely in an effort to expedite prosecution, claims reciting inverted repeats have been deleted. In addition, while Fitzmaurice et al. does suggest the use of STMV-derived vectors for introducing anti-sense RNA into plant cells for "blocking, interrupting or interfering with nucleic acids in a target cell", such as viruses (p10, line 14-19), it is deficient in teaching or suggesting that STMV derived vectors (and in particular vectors

comprising sense RNA) can be used for silencing of endogenous (nuclear encoded) plant genes.

Masuta et al. relates to vectors derived from "satellite RNAs", which are known in the art to belong to a different class than "satellite viruses", and which are completely distinct in a range of characteristics. For example, satellite RNAs are encapsidated in the viral particle of the helper virus, while satellite viruses are encapsidated in a separate viral particle than the helper virus. Further, like Fitzmaurice et al., Masuta et al. relates to the introduction of viral anti-sense sequences into the plant cell in order to protect the plant from viral infection, and not to silencing of endogenous plant genes.

The deficiencies of the combined teaching of Fitzmaurice et al. and Masuta et al. and are not remedied by Grierson et al. According to the Examiner, "Grierson et al. teach constructs and methods for enhancing the inhibition of a target gene within an organism comprising inserting into the gene silencing vector an inverted repeat sequence of all or part of a polynucleotide region within the vector." However, Grierson et al. neither teach nor suggest that silencing of endogenous genes can be obtained by satellite-virus derived RNA vectors comprising sense inhibitory RNA.

Hence, the combined teachings of Fitzmaurice et al., Masuta et al. and Grierson et al. do not motivate the person skilled in the art to modify the vectors of Fitzmaurice et al. into the vectors of the present invention, nor was there was a reasonable expectation that satellite RNA viruses, such as STMV or STNV, modified to comprise sense RNA, could be successfully used for silencing of nuclear encoded (endogenous) plant genes.

Moreover, it is submitted by the Applicants that prior to the filing of the present invention the use of satellite viruses as silencing vectors was generally doubted by persons skilled in the art, as such vectors were believed to be unstable (i.e. losing the exogenous sequence during replication) and as satellite viruses were known to have a high mutation rate.

In view of the above, withdrawal of this rejection is respectfully requested.

Conclusion

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is respectfully requested.

In the event that there are any questions concerning the present Amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Malcolm K. McGowan, Ph.D.
Registration No. 39,300

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: May 14, 2002

Attachment to Reply & Amendment dated May 14, 2002

Marked-up Claims 32, 34, 38, 39, 42, 43, 45, 49 and 50

32. (**amended**) A method for silencing endogenous genes by the introduction of inhibitory RNA in the cytoplasm of plant cells, said method comprising:

a) introducing into said plant cell, a viral RNA vector derived from a satellite RNA virus, wherein said vector comprises[ing] said inhibitory RNA or [comprising] a chimeric nucleic acid which when transcribed yields said inhibitory RNA and wherein said inhibitory RNA comprises sense RNA [, wherein said viral RNA vector is derived from a satellite RNA virus]; and

b) introducing a corresponding helper virus into said plant cell.

34. (**amended**) The method of claim 32, wherein said inhibitory RNA further comprises antisense RNA.

38. (**amended**) The method of claim 32, wherein said viral RNA vector is derived from STMV [and comprises an origin of assembly of tobacco mosaic virus,] and wherein said helper virus is tobacco mosaic virus.

39. (**amended**) [The] A method [of claim 32,] for the introduction of inhibitory RNA into the cytoplasm of plant cells, said method comprising:

a) introducing into said plant cell a [wherein said] viral RNA vector [is] derived from satellite tobacco necrosis virus, wherein said vector [and] comprises said inhibitory RNA, or a chimeric nucleic acid which when transcribed yields said inhibitory RNA, and an origin of assembly of tobacco mosaic virus; and

b) introducing a corresponding helper virus into said plant cell, wherein said helper virus is derived from tobacco necrosis virus and comprises a coat protein gene of tobacco mosaic virus.

42. (**amended**) The method of any one of claims 32, 34, 38 and 39 to 41, wherein said plant is selected from Nicotinia spp, Oryza sativa, Zea Mays, Brassica spp., Gossypium spp., Triticum spp., Arabidopsis spp. or Petunia spp.

43. (**amended**) A kit for silencing endogenous genes by introduction of inhibitory RNA in the cytoplasm of a plant cell, said kit comprising

a) a viral RNA vector derived from a satellite RNA virus, said vector comprising a chimeric nucleic acid which when transcribed yields said inhibitory RNA or which comprises said inhibitory RNA, wherein said inhibitory RNA comprises sense RNA; and

b) a corresponding helper virus.

45. (**amended**) The kit of claim 43, wherein said inhibitory RNA further comprises antisense RNA.

Attachment to Reply & Amendment dated May 14, 2002

Marked-up Claims 32, 34, 38, 39, 42, 43, 45, 49 and 50

49. (**amended**) The kit of claim 43, wherein said viral RNA vector is derived from STMV [and comprises an origin of assembly of tobacco mosaic virus,] and wherein said corresponding helper virus is tobacco mosaic virus.

50. (**amended**) [The] A kit [of claim 43,] for introduction of inhibitory RNA into the cytoplasm of a plant cell, said kit comprising:

a) a [wherein said] viral RNA vector [is] derived from satellite tobacco necrosis virus, wherein said vector [and] comprises said inhibitory RNA, or a chimeric nucleic acid which when transcribed yields said inhibitory RNA, and an origin of assembly of tobacco mosaic virus; and

b) a [wherein said] corresponding helper virus [is] derived from tobacco necrosis virus [and comprises], said virus comprising the coat protein gene of tobacco mosaic virus.